DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98D–0994]

Draft Guidance for Industry on BACPAC I: Intermediates in Drug Substance Synthesis; Bulk Actives Postapproval Changes: Chemistry, Manufacturing, and Controls Documentation; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''BACPAC I: Intermediates in Drug Substance Synthesis; Bulk Actives Postapproval Changes: Chemistry, Manufacturing, and Controls Documentation.'' This draft guidance provides recommendations to sponsors of new drug applications, abbreviated new drug applications, new animal drug applications, abbreviated new animal drug applications, and holders of drug master files or veterinary master files who intend, during the postapproval period, to change the site of manufacture, the scale of manufacture, the equipment, the specifications, and/or the manufacturing process of intermediates in the synthetic pathway leading to the drug substance.

DATES: Written comments on the draft guidance may be submitted by (*insert date 120 days after date of publication in the* **Federal Register**). General comments on the agency guidance documents are welcome at any time.

ADDRESSES: Copies of this draft guidance are available on the Internet at ''http://www.fda.gov/cder/guidance/index.htm'' or ''http://www.fda.gov/cvm''. Submit written requests for single copies of the draft guidance to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send

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one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments should be identified with the docket number found in brackets in the heading of this document.

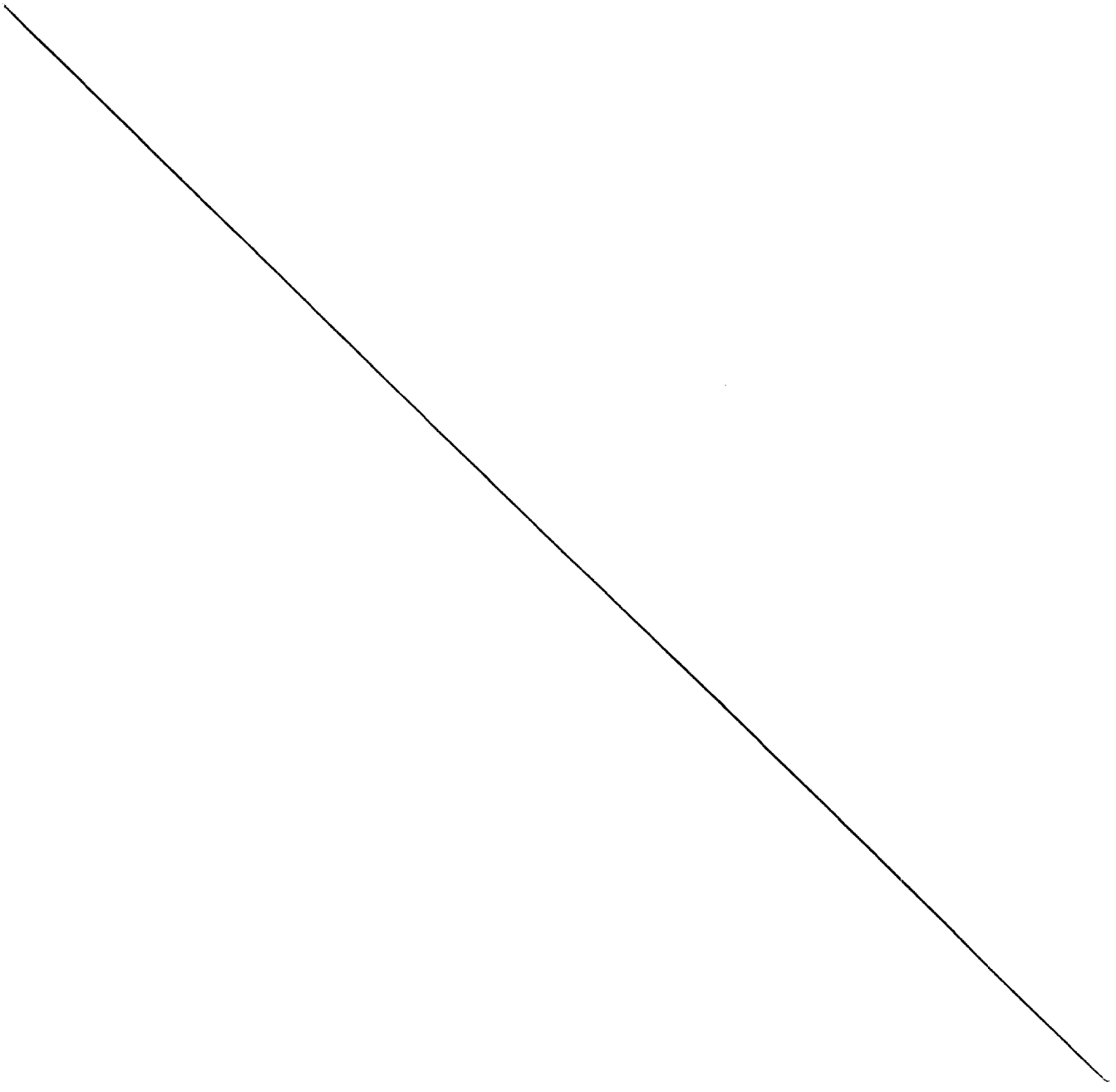
FOR FURTHER INFORMATION CONTACT: Kasturi Srinivasachar, Center for Drug Evaluation and Research (HFD–110), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5376, or David R. Newkirk, Center for Veterinary Medicine (HFV–142), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–2701.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a draft guidance entitled ''BACPAC I: Intermediates in Drug Substance Synthesis; Bulk Actives Postapproval Changes: Chemistry, Manufacturing, and Controls Documentation.'' This draft guidance defines recommended chemistry, manufacturing and controls tests, and documentation in support of each change. The draft guidance applies to synthetic drug substances and the synthetic steps involved in the preparation of semisynthetic drug substances. It is limited to structurally well-characterized drug substances where impurities can be monitored at the levels recommended. The draft guidance covers changes as follows: (1) Site, scale, and equipment changes involving the synthetic steps up to and including the step that produces the final intermediate, (2) specification changes for raw materials, starting materials, and intermediates, excluding the final intermediate, and (3) manufacturing process changes involving the synthetic steps up to and including the final intermediate. Postapproval changes affecting: (1) Synthetic peptides, (2) oligonucleotides, (3) radiopharmaceuticals, or (4) drug substances derived exclusively by isolation from natural sources or produced by procedures involving biotechnology are not addressed in this document.

This draft level 1 guidance is being issued consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). The draft guidance represents the agency's current thinking on postapproval changes for the manufacture of intermediates in drug substance syntheses. It does not create or confer any rights for or on any person and does not operate to bind FDA or the

public. An alternative approach may be used if such approach satisfies the requirement of the applicable statute, regulations, or both.

Interested persons may submit written comments on the draft guidance to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number



found in brackets in the heading of this document. The draft guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: November 20, 1998

November 20, 1998

William K. Hubbard
Associate Commissioner for Policy Coordination

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